DEPARTMENT OF HEALTH & HUMAN SERVICES

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Food and Drug Administration
Denver District Office
Building 20 – Denver Federal Center
P.O. Box 25087
Denver, Colorado 80225-0087
TELEPHONE: 303-236-3000

December 20, 1999

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Craig N. Thatcher, President
Thatcher Company
1900 Fortune Road
Salt Lake City, UT 84104

WARNING LETTER

Dear Mr. Thatcher:

This is regarding an inspection of your active pharmaceutical ingredient (API) manufacturing facility located in Salt Lake City, Utah by the U. S. Food and Drug Administration between the dates of April 15 and April 20, 1999. The inspection revealed significant deviations from current good manufacturing practices (CGMP) in the manufacture of APIs, and resulted in the issuance of an FDA Form 483, List of Observations, to you at the completion of the inspection. These deviations cause these APIs to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act. Section 501(a)(2)(B) of the Act requires that all drugs be manufactured, processed, packed, and held according to current good manufacturing practices. No distinction is made between active pharmaceutical ingredients and finished pharmaceuticals, and failure of either to comply with CGMP constitutes a failure to comply with the requirements of the Act.

Specific areas of concern found during the inspection include, but are not limited to:

1. Batch production records are incomplete or inadequate as evidenced by the batch record for [redacted] lot #97-4705, which failed to include: laboratory results which rejected the lot; record of the investigation in follow-up to this lot's failure; finished test results for pH, appearance and specific gravity; adequate calculation of needed raw materials to complete the manufacturing process; specific filter and packaging container to be used; and label reconciliation.

2. Investigations of non-conforming materials are inadequate in that the investigation following the rejection of [redacted] lot #97-4705, failed to state the actual reason for the rejection nor does it address the actual cause of the problem or

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appropriate corrective action to prevent similar failures in the future.

3. Investigation of [redacted] lot #97-6153, which fell out of specification during stability testing was inadequate in that it did not include a review of records and manufacturing procedures for deviations or errors, including assessing the potentially negative impact of storing the product in temporary containers for over 30 days while additional ingredients were ordered.

4. The stability program is inadequate in that there is no stability protocol for [redacted]; established stability testing points (i.e., 0, 6, 12, 24 months) are inappropriate; lots are not tested at scheduled test dates; there is no supporting data demonstrating comparability between containers used to store product on stability studies and the finished API product; and room temperature specifications of [redacted] are inappropriate for controlled stability studies.

5. Raw material testing is inadequate in that full characterization, including related substances has not been performed on [redacted] which is received from 2 separate vendors and contains from [redacted] related substances.

6. The [redacted], used to automatically control time and temperature settings during the [redacted] manufacturing process, has not been validated. Additionally these times and temperatures are not listed in the batch record nor are they monitored to insure these settings are met.

We have received and reviewed your response letter dated July 6, 1999. We find some of your responses to the FDA-483, issued to you on April 20, 1999, to be inadequate.

Your response to Observation 1, regarding the deficient batch record for [redacted], lot 97-4705, is inaccurate because "the paperwork" (batch production record) did not indicate that the batch was rejected. The Non-Conforming Material Reports were not included in the batch production records.

Your response to Observation 2, regarding inadequate investigations into non-conforming material, does not address the fact that these investigation reports are not included in the affected batch records.

Moreover, your response to Observation 2-b is unsatisfactory. If your product is formulated "near the lower limit of acceptable product specification," then you are not formulating with the intent to provide not less than 100 percent of the labeled amount of active ingredient.

Your response to Observation 6 reports that you do have a stability protocol for [redacted] in SOP [redacted] This is not adequate because the protocol which you reference is a generic protocol for all products and is not specific to characteristics of [redacted]

Your response to Observation 7 specifies that the [redacted] is "certified" every 6 months. It's not clear from your response as to whether the "certification" includes the required elements of validation of this computer's manufacturing functions.

Finally, in your response, your use of the terms "apparent" and "seemed obvious" does not alleviate you from the need to document manufacturing deviations in the batch production records.

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence with each requirement of the good manufacturing practices regulation. We recommend that you conduct a complete revaluation of your facility for CGMP compliance.

Due to the deficiencies listed on the FDA-483 provided to you at the conclusion of the inspection we are recommending to the Center for Drug Evaluation and Research that approval of your facility as an alternate supplier of [redacted] under a pending New Drug Application submitted by [redacted] be withheld.

Federal agencies are advised of the issuance of all warning letters about drugs and devices so that they may take this information into account when considering the award of contracts.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. This includes seizure and/or injunction.

Your reply should be sent to the Food and Drug Administration, Denver District Office, P.O. Box 25087, Denver, Colorado, 80225-0087, attention H. Tom Warwick, Compliance Officer. He may be reached at (303) 236-3054 if you have any questions about this matter.

Sincerely,

Gary C. Dean

Gary C. Dean
District Director